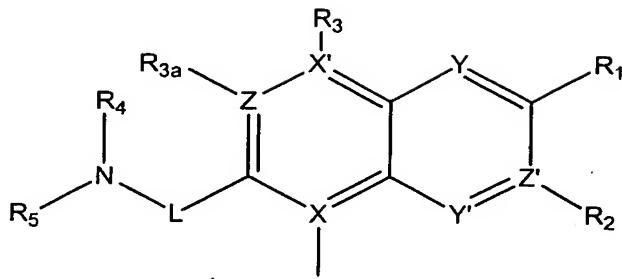


**WHAT IS CLAIMED IS:**

1. A compound of the formula:



(I)

5

or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof, wherein:

Y, and Y' are each independently selected from the group consisting of CH, CF, and N;

X, X', Z, and Z' are each independently C or N;

10 one of R<sub>1</sub> and R<sub>2</sub> is selected from the group consisting of halogen, cyano, and L<sub>2</sub>R<sub>6</sub>;

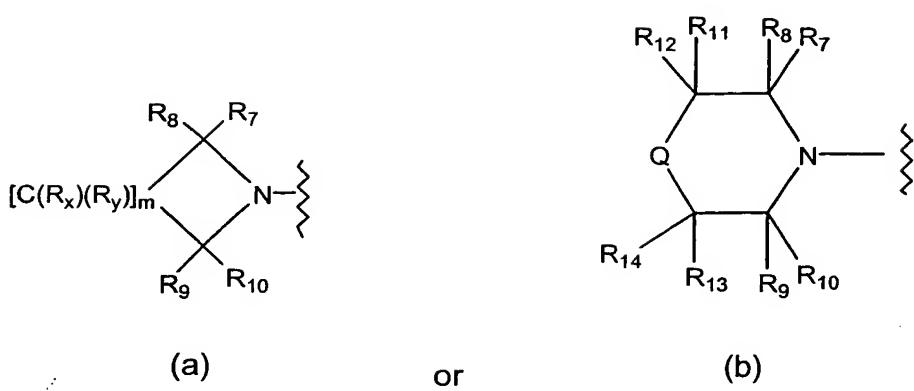
the other of R<sub>1</sub> and R<sub>2</sub> is selected from the group consisting of hydrogen, alkyl, alkoxy, aryl, cycloalkyl, halogen, cyano, and thioalkoxy, provided that R<sub>2</sub> is absent when Z' is N;

15 R<sub>3</sub> is absent when X' is N or R<sub>3</sub> is selected from the group consisting of hydrogen, alkyl, alkoxy, halogen, cyano, and thioalkoxy;

R<sub>3a</sub> is absent when Z is N or R<sub>3a</sub> is selected from the group consisting of hydrogen, methyl, alkoxy, halogen, and cyano;

20 R<sub>3b</sub> is absent when X is N or R<sub>3b</sub> is selected from the group consisting of hydrogen, alkyl, alkoxy, halogen, hydroxy, cyano, and thioalkoxy;

R<sub>4</sub> and R<sub>5</sub> are each independently selected from the group consisting of alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, and (NR<sub>A</sub>R<sub>B</sub>)alkyl, or R<sub>4</sub> and R<sub>5</sub> taken together with the nitrogen atom to which each is attached form a non-aromatic ring of the formula:



R<sub>6</sub> is selected from the group consisting of aryl, heteroaryl, heterocycle, and cycloalkyl;

R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub>, and R<sub>10</sub> at each occurrence are each independently selected

- 5 from the group consisting of hydrogen, hydroxyalkyl, fluoroalkyl, and alkyl; or one of the pair R<sub>7</sub> and R<sub>8</sub> or the pair R<sub>9</sub> and R<sub>10</sub> is taken together to form a C<sub>3</sub>-C<sub>6</sub> ring, wherein 0, 1, or 2 heteroatoms selected from O, N, or S replace a carbon atom in the ring;

- 10 R<sub>11</sub>, R<sub>12</sub>, R<sub>13</sub>, and R<sub>14</sub> are each independently selected from the group consisting of hydrogen, hydroxy, hydroxyalkyl, alkyl, and fluoro;

Q is selected from the group consisting of a bond, O, S, and NR<sub>15</sub>;

L is  $-[C(R_{16})(R_{17})]_n-$  or  $-[C(R_{16})(R_{17})]_pO-$ ;

L<sub>2</sub> is selected from the group consisting of a bond, -O-, -C(=O)-, -S-,  $-[C(R_{18})(R_{19})]_q-$ , -O-[C(R<sub>18</sub>)(R<sub>19</sub>)]<sub>q</sub>-, -NH- and -N(alkyl)-;

- 15 R<sub>15</sub> is selected from the group consisting of hydrogen, alkyl, acyl, amido, and formyl;

R<sub>16</sub> and R<sub>17</sub> at each occurrence are independently selected from the group consisting of hydrogen, alkyl, alkoxy, and fluoro;

- 20 R<sub>18</sub> and R<sub>19</sub> at each occurrence are each independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkoxy, and fluoro;

R<sub>x</sub> and R<sub>y</sub> at each occurrence are independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkoxy, alkylamino, dialkylamino, and fluoro, or one of R<sub>x</sub> or R<sub>y</sub> represents a covalent bond when taken together with R<sub>x</sub> or R<sub>y</sub> on an adjacent carbon atom such that a double bond is represented between the adjacent carbon atoms;

m is an integer from 1 to 5;

- n is an integer from 1 to 6;  
p is an integer from 2 to 6; and  
q is an integer from 1 to 4;  
wherein 0, 1, or 2 of X, X', Y, Y', Z, and Z' can be nitrogen; provided that R<sub>3</sub>  
5 is absent when X' is N; R<sub>3a</sub> is absent when Z is N; R<sub>2</sub> is absent when Z' is N, and  
R<sub>3b</sub> is absent when X is N.
2. The compound of claim 1, wherein R<sub>1</sub> is bromo, cyano, or L<sub>2</sub>R<sub>6</sub>.
- 10 3. The compound of claim 1, wherein R<sub>1</sub> is L<sub>2</sub>R<sub>6</sub>, L<sub>2</sub> is -CH(OH)-, -C(=O)-, or a  
bond, and R<sub>6</sub> is aryl, heteroaryl, heterocycle, or cycloalkyl.
4. The compound of claim 1, wherein R<sub>1</sub> is L<sub>2</sub>R<sub>6</sub>, L<sub>2</sub> is a bond, and R<sub>6</sub> is aryl  
wherein the aryl is phenyl substituted with 0, 1, or 2 substituents selected from the  
15 group consisting of cyano, halogen, -NR<sub>A</sub>R<sub>B</sub>, alkoxy, hydroxylalkyl, alkylcarbonyl,  
alkoxycarbonyl, cycloalkylcarbonyl, alkylsulfonyl, haloalkyl, and thioalkoxy.
5. The compound of claim 1, wherein R<sub>1</sub> is L<sub>2</sub>R<sub>6</sub>, L<sub>2</sub> is a bond, and R<sub>6</sub> is  
selected from the group consisting of furyl, imidazolyl, isothiazolyl, isoxazolyl,  
20 oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridazinonyl, pyridinonyl,  
pyridinyl, pyrimidinyl, pyrrolyl, tetrazolyl, thiadiazolyl, thiazolyl, thienyl, triazinyl,  
and triazolyl, substituted with 0, 1, 2, or 3 substituents selected from the group  
consisting of -NR<sub>A</sub>R<sub>B</sub>, halogen, alkyl, cyano, alkoxyimino, alkoxy carbonyl,  
25 (NR<sub>A</sub>R<sub>B</sub>) carbonyl, alkylcarbonyl, haloalkyl, and alkoxy.
6. The compound of claim 1, wherein R<sub>1</sub> is L<sub>2</sub>R<sub>6</sub>, L<sub>2</sub> is a bond, and R<sub>6</sub> is  
selected from the group consisting of azepanyl, azetidinyl, aziridinyl, azocanyl,  
dihydrothiazolyl, morpholinyl, piperazinyl, piperidinyl, pyrrolidinyl, pyrrolinyl,  
thiomorpholinyl, tetrahydropyridinyl, tetrahydrofuryl, and tetrahydropyranyl.
- 30 7. The compound of claim 1, wherein R<sub>4</sub> and R<sub>5</sub> are each independently  
selected from methyl, ethyl, and propyl.

8. The compound of claim 1, wherein R<sub>4</sub> and R<sub>5</sub> taken together with the nitrogen atom to which each is attached form a 4- to 8-membered non-aromatic ring represented by formula (a).
- 5 9. The compound of claim 8, wherein the 4- to 8-membered non-aromatic ring is selected from the group consisting of azetidinyl, azepanyl, azepinyl, pyrrolidinyl, pyrrolinyl, piperidinyl, piperazinyl, and tetrahydropyridinyl, substituted with 0, 1, or 2 substituents selected from the group consisting of alkyl, hydroxyalkyl, fluoroalkyl, and -NR<sub>A</sub>R<sub>B</sub>.
- 10 10. The compound of claim 8, wherein at least one substituent represented by R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub>, and R<sub>10</sub> is selected from the group consisting of alkyl, halogen, fluoroalkyl, and hydroxyalkyl or at least one substituent represented by R<sub>x</sub> or R<sub>y</sub> is selected from the group consisting of hydrogen, hydroxy, and fluoro.
- 15 11. The compound of claim 8, wherein the 4- to 8-membered non-aromatic ring is selected from the group consisting of methylpyrrolidinyl, ethylpyrrolidinyl, dimethylaminopyrrolidinyl, isopropylpyrrolidinyl, isobutylpyrrolidinyl, hydroxymethylpyrrolidinyl, and fluoromethylpyrrolidinyl.
- 20 12. The compound of claim 1, wherein R<sub>4</sub> and R<sub>5</sub> taken together with the nitrogen atom to which each is attached form morpholinyl or thiomorpholinyl.
- 25 13. The compound of claim 1, wherein at least one substituent represented by R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub>, and R<sub>10</sub> is hydroxyalkyl, fluoroalkyl, or alkyl.
14. The compound of claim 1, wherein at least one substituent represented by R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub>, and R<sub>10</sub> is methyl, ethyl, fluoromethyl, or hydroxymethyl.
- 30 15. The compound of claim 1, wherein one substituent represented by R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub>, and R<sub>10</sub> is alkyl and the other three substituents are hydrogen.

16. The compound of claim 1, wherein R<sub>11</sub>, R<sub>12</sub>, R<sub>13</sub>, and R<sub>14</sub> are each hydrogen.
17. The compound of claim 1, wherein R<sub>11</sub> and R<sub>12</sub> each are hydrogen, and R<sub>13</sub> and R<sub>14</sub> are each independently selected from the group consisting of hydrogen and alkyl.
18. The compound of claim 1, wherein R<sub>15</sub> is selected from the group consisting of hydrogen, alkyl, amido, and formyl.
19. The compound of claim 1, wherein R<sub>16</sub> and R<sub>17</sub> are hydrogen.
20. The compound of claim 1, wherein R<sub>18</sub> and R<sub>19</sub> are hydrogen.
21. The compound of claim 1, wherein m is 2 or 3.
22. The compound of claim 1, wherein n is 2 or 3.
23. The compound of claim 1, wherein p is 2.
24. The compound of claim 1, wherein q is 1.
25. The compound of claim 1, wherein Y and Y' are CH; X, X', Z, and Z' are C; and R<sub>2</sub>, R<sub>3</sub>, R<sub>3a</sub>, and R<sub>3b</sub> are hydrogen.
26. The compound of claim 1, wherein Y and Y' are CH; X, X', and Z are C; R<sub>3</sub>, R<sub>3a</sub>, and R<sub>3b</sub> are hydrogen; Z' is N; and R<sub>2</sub> is absent.

27. The compound of claim 1, wherein  
Y and Y' are CH;  
X', Z', and Z are C;  
5 R<sub>2</sub>, R<sub>3</sub>, and R<sub>3a</sub> are hydrogen;  
X is N; and  
R<sub>3b</sub> is absent.
28. The compound of claim 1, wherein  
10 Y and Y' are CH;  
X, X', and Z' are C;  
R<sub>2</sub>, R<sub>3</sub>, and R<sub>3b</sub> are hydrogen;  
Z is N; and  
R<sub>3a</sub> is absent.
- 15 29. The compound of claim 1, wherein  
Y is CH;  
X, X', Z, and Z' are C;  
R<sub>2</sub>, R<sub>3</sub>, R<sub>3a</sub>, and R<sub>3b</sub> are hydrogen; and  
20 Y' is N.
30. The compound of claim 1, wherein  
Y and Y' are CH;  
X and Z' are C;  
25 R<sub>2</sub> and R<sub>3b</sub> are hydrogen;  
X' is N;  
Z is N; and  
R<sub>3</sub> and R<sub>3a</sub> are absent.
- 30 31. The compound of claim 1, wherein  
X, X', Z, and Z' are C;  
R<sub>2</sub>, R<sub>3</sub>, R<sub>3a</sub>, and R<sub>3b</sub> are hydrogen;  
Y is N; and

Y' is N.

32. The compound of claim 1, wherein

Y' is CH;

5 X, X', and Z are C;

R<sub>3</sub>, R<sub>3a</sub>, and R<sub>3b</sub> are hydrogen;

Y is N;

Z' is N; and

R<sub>2</sub> is absent.

10

33. The compound of claim 1, wherein

Y' is CH;

X, Z, and Z' are C;

R<sub>2</sub>, R<sub>3a</sub>, and R<sub>3b</sub> are hydrogen;

15

Y is N;

X' is N; and

R<sub>3</sub> is absent.

34. The compound of claim 1, wherein

20

Y' is CH;

X, X', and Z' are C;

R<sub>2</sub>, R<sub>3</sub>, and R<sub>3b</sub> are hydrogen;

Y is N;

Z is N; and

25

R<sub>3a</sub> is absent.

35. The compound of claim 1, wherein

Y is CH;

X, X', and Z are C;

30

R<sub>3</sub>, R<sub>3a</sub>, and R<sub>3b</sub> are hydrogen;

Y' is N;

Z' is N; and

R<sub>2</sub> is absent.

36. The compound of claim 1, wherein  
Y and Y' are CH;  
Z' and Z are C;
- 5 R<sub>2</sub> and R<sub>3a</sub> are hydrogen;  
X' is N;  
X is N; and  
R<sub>3</sub> and R<sub>3b</sub> are absent.
- 10 37. The compound of claim 1, wherein  
Y' is CH;  
X, X', Z and Z' are C;  
R<sub>2</sub>, R<sub>3</sub>, R<sub>3a</sub>, and R<sub>3b</sub> are hydrogen; and  
Y is N.
- 15 38. The compound of claim 1, wherein  
Y and Y' are CH;  
X' and Z' are C;  
R<sub>2</sub> and R<sub>3</sub> are hydrogen;  
20 X is N;  
Z is N; and  
R<sub>3a</sub> and R<sub>3b</sub> are absent.
39. The compound of claim 1, wherein  
25 Y is CH;  
X, Z', and Z are C;  
R<sub>2</sub>, R<sub>3a</sub>, and R<sub>3b</sub> are hydrogen;  
Y' is N;  
X' is N; and  
30 R<sub>3</sub> is absent.
40. The compound of claim 1, wherein:  
R<sub>1</sub> is L<sub>2</sub>R<sub>6</sub> wherein L<sub>2</sub> is a bond and R<sub>6</sub> is heteroaryl or heterocycle;

R<sub>2</sub>, R<sub>3</sub>, R<sub>3a</sub>, and R<sub>3b</sub> are hydrogen;

L is -[C(R<sub>16</sub>)(R<sub>17</sub>)]<sub>n</sub>-;

n is 2;

R<sub>16</sub> and R<sub>17</sub> at each occurrence are hydrogen;

5 R<sub>4</sub> and R<sub>5</sub> are taken together to form a methylpyrrolidinyl ring of formula

(a), wherein one of R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub>, and R<sub>10</sub> is methyl and the remaining three substituents are hydrogen;

Y and Y' are CH; and

X, X', Z, and Z' are C.

10

41. The compound of claim 40, wherein R<sub>1</sub> is a heteroaryl group selected from 2H-pyridazin-3-one-2-yl.

42. The compound of claim 1, selected from the group consisting of

15 4-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)benzonitrile;

(2R)-1-[2-(6-bromo-2-naphthyl)ethyl]-2-methylpyrrolidine;

1-[3-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)phenyl]ethanone;

2-[3-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)phenyl]-2-

propanol;

20 6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthonitrile;

4-(6-{[(2R)-2-methyl-1-pyrrolidinyl]methyl}-2-naphthyl)benzonitrile;

3-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)benzonitrile;

4-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)pyridine;

3-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)pyridine;

25 (3-fluorophenyl)(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-

naphthyl)methanol;

3,5-dimethyl-4-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-

naphthyl)isoxazole;

4-(6-{2-[(2S)-2-(hydroxymethyl)-1-pyrrolidinyl]ethyl}-2-naphthyl)benzonitrile;

30 4-(6-{2-[(3R)-3-hydroxy-1-pyrrolidinyl]ethyl}-2-naphthyl)benzonitrile;

4-{6-[2-(2-isobutyl-1-pyrrolidinyl)ethyl]-2-naphthyl}benzonitrile;

4-{6-[2-(2-isopropyl-1-pyrrolidinyl)ethyl]-2-naphthyl}benzonitrile;

4-(6-{2-[(3R)-3-(dimethylamino)-1-pyrrolidinyl]ethyl}-2-naphthyl)benzonitrile;

4-{6-[2-(diethylamino)ethyl]-2-naphthyl}benzonitrile;  
4-{6-[2-(dimethylamino)ethyl]-2-naphthyl}benzonitrile;  
4-(6-{2-[ethyl(isopropyl)amino]ethyl}-2-naphthyl)benzonitrile;  
4-(6-{2-[tert-butyl(methyl)amino]ethyl}-2-naphthyl)benzonitrile;  
5 4-(6-{2-[(2S)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)benzonitrile;  
4-(6-{2-[(2R)-2-methyl-1-piperidinyl]ethyl}-2-naphthyl)benzonitrile;  
4-{6-[2-(2,5-dihydro-1*H*-pyrrol-1-yl)ethyl]-2-naphthyl}benzonitrile;  
4-(6-{2-[methyl(propyl)amino]ethyl}-2-naphthyl)benzonitrile;  
4-(6-{2-[(2-hydroxyethyl)(methyl)amino]ethyl}-2-naphthyl)benzonitrile;  
10 5-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)pyrimidine;  
4-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)morpholine;  
2-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)-1,3-thiazole;  
4-(6-{2-[(2S)-2-(fluoromethyl)-1-pyrrolidinyl]ethyl}-2-naphthyl)benzonitrile;  
15 (3-fluorophenyl)(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)methanone;  
2-6-{2-[(2R)-2-methyl-1-pyrrolidin-1-yl]-ethyl}-2-naphthalen-2-yl)-2*H*-  
pyridazin-3-one;  
2-methoxy-5-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)pyridine;  
4-(6-{2-[(2R)-2-(hydroxymethyl)-1-pyrrolidinyl]ethyl}-2-naphthyl)benzonitrile;  
20 4-{6-[2-(2-methyl-1-pyrrolidinyl)ethyl]-2-naphthyl}benzonitrile;  
4-{6-[2-(1-pyrrolidinyl)ethyl]-2-naphthyl}benzonitrile;  
4-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)thiomorpholine;  
1-{2-[(6-bromo-2-naphthyl)oxy]ethyl}pyrrolidine;  
25 3-{6-[2-(1-pyrrolidinyl)ethoxy]-2-naphthyl}benzonitrile;  
3-{6-[2-(1-pyrrolidinyl)ethoxy]-2-naphthyl}pyridine;  
3-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethoxy}-2-naphthyl)benzonitrile;  
3-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethoxy}-2-naphthyl)pyridine;  
4-(2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-6-quinolinyl)benzonitrile;  
30 6-(4-fluorophenyl)-2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}quinoline;  
3-(2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-6-quinolinyl)benzonitrile;  
1-[3-(2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-6-quinolinyl)phenyl]ethanone;  
6-(4-methoxyphenyl)-2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}quinoline;

- 2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-6-[4-(trifluoromethyl)phenyl]quinoline;  
2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-6-[4-(methylsulfonyl)phenyl]quinoline;
- 5 6-(3,5-difluorophenyl)-2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}quinoline;  
(3-fluorophenyl)(2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-6-quinolinyl)methanone;  
2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-6-(3-pyridinyl)quinoline;  
4-(3-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-7-isoquinolinyl)benzonitrile;
- 10 3-(3-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-7-isoquinolinyl)benzonitrile;  
6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-(3-pyridinyl)quinoline;  
6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-(4-pyridinyl)quinoline;  
6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-(2-pyridinyl)quinoline;  
6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-(1,3-thiazol-2-yl)quinoline;
- 15 2-(2,4-dimethyl-1,3-thiazol-5-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}quinoline;  
6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-(2-pyrazinyl)quinoline;  
1-[6-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-quinolinyl)-2-pyridinyl]ethanone;
- 20 4-(2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-6-quinoxalinyl)benzonitrile;  
4-(3-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-6-quinoxalinyl)benzonitrile;  
7-(2,6-difluoro-3-pyridinyl)-3-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}isoquinoline;  
3-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-7-(3-pyridinyl)isoquinoline;
- 25 3-(benzyloxy)-2-methyl-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}quinoline;  
2-cyclopropyl-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}quinoline;  
4-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-quinolinyl)benzonitrile;  
2,6-dimethyl-5-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-quinolinyl)nicotinonitrile;
- 30 2-(3-methyl-2-pyrazinyl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}quinoline;  
ethyl 5-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-quinolinyl)-3-isoxazolecarboxylate;

5-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-quinolinyl)-2-thiophenecarbonitrile;  
ethyl 5-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-quinolinyl)-2-thiophenecarboximidoate;

5 2-(2,4-dimethyl-1,3-oxazol-5-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}quinoline;  
ethyl 3-methyl-5-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-quinolinyl)-4-isoxazolecarboxylate;  
4-(7-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-3-isoquinoliny)benzonitrile;

10 6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-(4-methoxyphenyl)quinoxaline;  
7-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-(4-methoxyphenyl)quinoxaline;  
6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-phenylquinoxaline;  
7-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-phenylquinoxaline;  
6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-(3-pyridinyl)quinazoline;

15 6-methyl-2-{6-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-2H-pyridazin-3-one;  
5-{6-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-pyrimidine-2-carbonitrile;  
1-{6-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-1H-pyridin-2-one;

20 5-{6-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-nicotinonitrile;  
4-methyl-1-{6-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-1H-pyridin-2-one;  
2-{6-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-pyrazine;

25 2-{6-[2-((2R)-2-methyl-2,5-dihydro-pyrrol-1-yl)-ethyl]-naphthalen-2-yl}-2H-pyridazin-3-one;  
4-(6-{2-[(2-dimethylamino-ethyl)-methyl-amino]-ethyl}-naphthalen-2-yl)-benzonitrile;  
4-{6-[2-(4-methyl-piperazin-1-yl)-ethyl]-naphthalen-2-yl}-benzonitrile;

30 2-(2,5-dimethyl-furan-3-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-quinoline;  
6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-(4-methylsulfanyl-phenyl)-quinoline;

- 2-(6-methyl-pyridin-3-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-quinoline;  
2-(1,3-dimethyl-1*H*-pyrazol-4-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-  
quinoline;  
6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-thiophen-3-yl-quinoline;  
5 6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-pyrimidin-5-yl-quinoline;  
2-(2,6-dimethyl-pyridin-3-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-  
quinoline;  
1-[2,6-dimethyl-5-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-quinolin-2-yl)-  
pyridin-3-yl]-ethanone.;  
10 6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-(2*H*-pyrazol-3-yl)-quinoline;  
2-(3-bromo-isoxazol-5-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-quinoline;  
2-(6-chloro-pyridin-3-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-quinoline;  
2-(3,5-dimethyl-thiophen-2-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-  
quinoline;  
15 6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-thiophen-2-yl-quinoline;  
2-furan-3-yl-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-quinoline;  
2-(4,5-dihydro-thiazol-2-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-  
quinoline;  
1-[4-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-quinolin-2-yl)-phenyl]-  
20 ethanone;  
3-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-quinolin-2-yl)-2-trifluoromethyl-  
pyridin-4-ol;  
2-(3,5-dimethyl-1*H*-pyrazol-4-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-  
quinoline;  
25 6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-(1*H*-pyrazol-4-yl)-quinoline;  
2,6-dimethyl-5-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-quinolin-2-yl)-  
nicotinamide;  
2-[2-(2R-methyl-pyrrolidin-1-yl)-ethyl]-6-pyridin-4-yl-quinoline;  
30 6-(6-methoxy-pyridin-3-yl)-2-[2(R)-(2-methyl-pyrrolidin-1-yl)-ethyl]-quinoline;  
6-(2,6-difluoro-pyridin-3-yl)-2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-  
quinoline;  
6-(6-chloro-pyridin-3-yl)-2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-quinoline;

- 6-(2,6-dichloro-pyridin-3-yl)-2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-quinoline;
- 2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-6-pyrazin-2-yl-quinoline;
- 2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-6-pyrimidin-5-yl-quinoline;
- 5 6-(2,4-dimethoxy-pyrimidin-5-yl)-2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-quinoline;
- dimethyl-(4-{2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-quinolin-6-yl}-phenyl)-amine;
- 10 1-(4-{2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-quinolin-6-yl}-phenyl)-ethanone;
- 6-(4-chloro-phenyl)-2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-quinoline;
- 6-(2,6-dimethyl-pyridin-3-yl)-2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-quinoline;
- 15 6-(5-methoxy-pyridin-3-yl)-2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-quinoline;
- 6-(3,5-dimethyl-isoxazol-4-yl)-2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-quinoline;
- 4-{2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-quinolin-6-yl}-benzoic acid methyl ester;
- 20 2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-6-(4-methylsulfanyl-phenyl)-quinoline;
- 6-(6-fluoro-pyridin-3-yl)-2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-quinoline;
- 5-{2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-quinolin-6-yl}-nicotinonitrile;
- 2,4-dimethoxy-5-{6-[2-((2R)-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-pyrimidine;
- 25 2,6-difluoro-3-{6-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-pyridine;
- cyclopropyl-(4-{6-[2-((2R)2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-phenyl)-methanone;
- 3-methoxy-6-{6-[2-((2R)2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-
- 30 pyridazine;
- 4-{6-[2-(2-methyl-piperidin-1-yl)-ethyl]-naphthalen-2-yl}-benzonitrile;
- 4-{6-[2-((2R)-2-ethyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-benzonitrile;

2-[6-[2-((2S)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl]-2H-pyridazin-3-one;

2-[6-((2R)-2-piperidin-1-yl-ethyl)-naphthalen-2-yl]-2H-pyridazin-3-one;

2-[6-[2-(tert-butyl-methyl-amino)-ethyl]-naphthalen-2-yl]-2H-pyridazin-3-one;

2-[6-(2-diethylamino-ethyl)-naphthalen-2-yl]-2H-pyridazin-3-one;

2-[6-(2-morpholin-4-yl-ethyl)-naphthalen-2-yl]-2H-pyridazin-3-one;

2-[6-[2-(ethyl-methyl-amino)-ethyl]-naphthalen-2-yl]-2H-pyridazin-3-one;

2-[6-[2-((2S)-2-fluoromethyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl]-2H-pyridazin-3-one;

2-[6-[2-(2-hydroxymethyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl]-2H-pyridazin-3-one;

2-[6-[2-((R)-2-ethyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl]-2H-pyridazin-3-one;

2-[6-(2-azetidin-1-yl-ethyl)-naphthalen-2-yl]-2H-pyridazin-3-one;

2-[6-[2-((2S)-2-fluoromethyl-azetidin-1-yl)-ethyl]-naphthalen-2-yl]-2H-pyridazin-3-one;

2-[6-[2-((2S)-2-hydroxymethyl-azetidin-1-yl)-ethyl]-naphthalen-2-yl]-2H-pyridazin-3-one;

2-[6-[2-((2R,5R)-2,5-Dimethyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl]-2H-pyridazin-3-one;

2-[6-[2-((2R,6S)-2,6-dimethyl-piperidin-1-yl)-ethyl]-naphthalen-2-yl]-2H-pyridazin-3-one;

2-[6-[2-((R)-3-hydroxy-piperidin-1-yl)-ethyl]-naphthalen-2-yl]-2H-pyridazin-3-one;

2-[6-[2-((R)-2-methyl-piperidin-1-yl)-ethyl]-naphthalen-2-yl]-2H-pyridazin-3-one;

2,6-dimethyl-3-[6-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl]-pyridine;

5-[6-[2-((R)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl]-thiazole;

2-[6-[2-((R)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl]-pyrimidine;

3-chloro-6-[6-[2-((R)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl]-pyridazine;

5-{6-[2-((R)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-pyrimidin-2-ylamine;

2-methyl-5-{6-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-pyridine;

5 3-bromo-7-(2-pyrrolidin-1-yl-ethyl)-[1,5]naphthyridine;

3-bromo-7-[2-(2R-2-methyl-pyrrolidin-1-yl)-ethyl]-[1,5]naphthyridine;

3-bromo-7-(2-piperidin-1-yl-ethyl)-[1,5]naphthyridine;

3-(2,6-dimethyl-pyridin-3-yl)-7-[2-(2R-2-methyl-pyrrolidin-1-yl)-ethyl]-[1,5]naphthyridine;

10 3-(2,4-dimethoxy-pyrimidin-5-yl)-7-[2-(2R-2-methyl-pyrrolidin-1-yl)-ethyl]-[1,5]naphthyridine;

3-(2,6-dimethyl-pyridin-3-yl)-7-(2-pyrrolidin-1-yl-ethyl)-[1,5]naphthyridine;

15 3-(2,4-dimethoxy-pyrimidin-5-yl)-7-(2-pyrrolidin-1-yl-ethyl)-[1,5]naphthyridine;

3-(2,6-dimethyl-pyridin-3-yl)-7-(2-piperidin-1-yl-ethyl)-[1,5]naphthyridine;

3-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-7-pyridin-4-yl-isoquinoline;

7-(6-methoxy-pyridin-3-yl)-3-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-

20 isoquinoline;

3-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-7-pyrimidin-5-yl-isoquinoline;

7-(6-fluoro-pyridin-3-yl)-3-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-isoquinoline;

5-{3-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-isoquinolin-7-yl}-nicotinonitrile;

7-(3-chloro-pyridin-4-yl)-3-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-

25 isoquinoline;

7-bromo-3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnolin-4-ol;

4-{3-[2-(2-methyl-pyrrolidin-1-yl)-ethyl]-cinnolin-7-yl}-benzonitrile;

7-bromo-4-chloro-3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnoline;

4-{4-hydroxy-3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnolin-7-yl}-

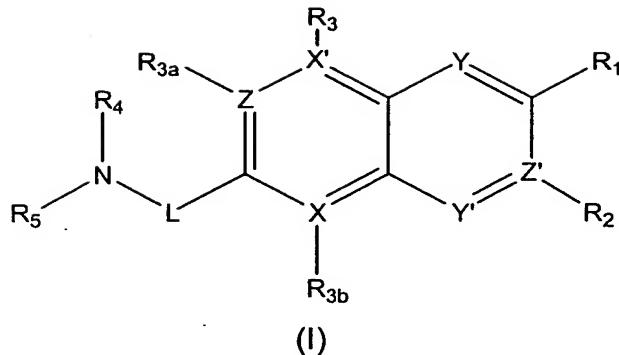
30 benzonitrile;

4-{4-isopropoxy-3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnolin-7-yl}-benzonitrile;

4-{3-[2-(4-methyl-piperazin-1-yl)-ethyl]-cinnolin-7-yl}-benzonitrile;

- 4-[3-(2-piperidin-1-yl-ethyl)-cinnolin-7-yl]-benzonitrile;  
4-[3-(2-pyrrolidin-1-yl-ethyl)-cinnolin-7-yl]-benzonitrile;  
4-{3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnolin-7-yl}-benzonitrile;  
4-{3-[2-((2R)-2-hydroxymethyl-pyrrolidin-1-yl)-ethyl]-cinnolin-7-yl}-  
5 benzonitrile;  
4-[3-(2-morpholin-4-yl-ethyl)-cinnolin-7-yl]-benzonitrile;  
4-{3-[2-(4-methyl-piperidin-1-yl)-ethyl]-cinnolin-7-yl}-benzonitrile;  
4-{3-[2-(ethyl-methyl-amino)-ethyl]-cinnolin-7-yl}-benzonitrile;  
7-(2,6-dimethyl-pyridin-3-yl)-3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-  
10 cinnoline;  
7-(2,4-dimethoxy-pyrimidin-5-yl)-3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-  
cinnoline;  
7-(6-methoxy-pyridin-3-yl)-3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-  
cinnoline;  
15 3-{3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnolin-7-yl}-benzonitrile;  
5-{3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnolin-7-yl}-nicotinonitrile;  
7-(4-fluoro-phenyl)-3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnoline;  
2-{3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnolin-7-yl}-pyrrole-1-  
carboxylic acid tert-butyl ester;  
20 (3-{3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnolin-7-yl}-phenyl)-  
methanol;  
7-(3,5-difluoro-phenyl)-3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnoline;  
3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-7-thiophen-3-yl-cinnoline;  
7-(4-chloro-phenyl)-3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnoline;  
25 7-(4-ethoxy-phenyl)-3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnoline;  
3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-7-(1*H*-pyrrol-2-yl)-cinnoline; and  
2-(1,5-dimethyl-1*H*-pyrazol-4-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-  
quinoline.  
  
30 43. The compound of claim 1, that is 2-(6-{2-[(2R)-2-methyl-1-pyrrolidin-1-yl]-  
ethyl}-2-naphthalen-2-yl)-2*H*-pyridazin-3-one or 2-(6-{2-[(2R)-2-methyl-1-  
pyrrolidinyl]ethyl}-2-naphthyl)-3(2*H*)-pyridazinone.

44. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 in combination with a pharmaceutically acceptable carrier.
- 5 45. A method of selectively modulating the effects of histamine-3 receptors in a mammal comprising administering an effective amount of a compound of claim 1.
46. A method of treating a condition or disorder modulated by the histamine-3 receptors in a mammal comprising administering an effective amount of a compound of claim 1.
- 10
47. The method according to claim 46, wherein the condition or disorder is selected from the group consisting of acute myocardial infarction, Alzheimer's disease, asthma, attention-deficit hyperactivity disorder, bipolar disorder, cognitive dysfunction, cognitive deficits in psychiatric disorders, deficits of memory, deficits of learning, dementia, cutaneous carcinoma, drug abuse, diabetes, type II diabetes, depression, epilepsy, gastrointestinal disorders, inflammation, insulin resistance syndrome, jet lag, medullary thyroid carcinoma, melanoma, Meniere's disease, metabolic syndrome, mild cognitive impairment, migraine, mood and 15 attention alteration, motion sickness, narcolepsy, neurogenic inflammation, obesity, obsessive compulsive disorder, pain, Parkinson's disease, polycystic ovary syndrome, schizophrenia, cognitive deficits of schizophrenia, seizures, septic shock, Syndrome X, Tourette's syndrome, vertigo, and sleep disorders.
- 20
- 25 48. The method according to claim 46, wherein the condition or disorder affects the memory or cognition.
49. The method according to claim 46, wherein the condition or disorder is Alzheimer's disease, attention-deficit hyperactivity disorder, schizophrenia, or 30 cognitive deficits of schizophrenia.
50. A process for preparing a compound of formula (I):



or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof, wherein:

R<sub>1</sub> is L<sub>2</sub>R<sub>6</sub> wherein L<sub>2</sub> is a bond and R<sub>6</sub> is 3(2H)-pyridazinon-2-yl;

R<sub>2</sub>, R<sub>3</sub>, R<sub>3a</sub>, and R<sub>3b</sub> are hydrogen;

5       L is -[C(R<sub>16</sub>)(R<sub>17</sub>)]<sub>n</sub>-;

n is 2;

R<sub>16</sub> and R<sub>17</sub> at each occurrence are hydrogen;

R<sub>4</sub> and R<sub>5</sub> are taken together to form a methylpyrrolidinyl ring of formula

(a), wherein one of R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub>, and R<sub>10</sub> is methyl and the remaining three

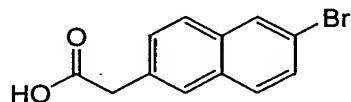
10      substituents are hydrogen;

Y and Y' are CH; and

X, X', Z, and Z' are C;

comprising the steps of:

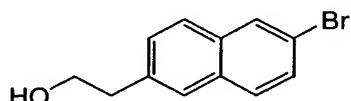
(a) providing a compound (II):



(II)

15

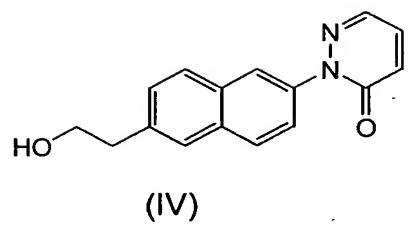
(b) reducing the compound (II) with BH<sub>3</sub>-THF to provide a compound (III):



(III)

15

(c) treating the compound of formula (III) with 3(2H)-pyridazinone, copper powder, and base to provide a compound (IV):



(d) activating the hydroxy group of compound (IV); and reacting the resulting compound with methylpyrrolidine to provide a compound of formula (I).